Perinatal management of infant tumors and the promise of fetal surgery

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Purpose of review
This review outlines the current approaches to prenatal imaging, differential diagnosis, antenatal natural history, and the available treatment options for the most commonly prenatally diagnosed malignant tumors.

Recent findings
In-utero diagnosis of fetal tumors, although still a rare event, has become more common as prenatal imaging modalities have improved. In general, this prenatal diagnosis allows more informed prenatal counseling and better perinatal planning for potentially high-risk deliveries. There are rare indications for prenatal fetal intervention.

Summary
Diagnosis of a fetal tumor should prompt referral to a specialized center. Further understanding of these rare patients will require multicenter collaboration.

Keywords
EXIT, fetal surgery, fetal tumor

INTRODUCTION

Significant advances in prenatal imaging by high-resolution ultrasound and ultrafast MRI have allowed us to more accurately diagnose fetal tumors which may be malignant or have malignant potential, or conditions which may predispose to the development of malignant tumors during postnatal life. This increase in prenatal diagnostic capability has significant benefits for the parents, the fetus, and the perinatal team taking care of these patients. Fetal and neonatal tumors have a range of outcomes depending on the anatomical site of origin, malignant potential, and response to treatment. For the parents of a fetus diagnosed with a neoplastic process, it affords more comprehensive prenatal counseling so that parents know what to expect for the duration of the pregnancy and can help prepare them for the challenges that the baby will face in the perinatal period and beyond. For the fetus, prenatal diagnosis has allowed us to identify a subset of these babies that have historically had a very poor prognosis. Lastly, for the perinatal team, prenatal diagnosis helps identify those high-risk patients who will have significant issues in the perinatal period to ensure that the baby is delivered in the appropriate setting, at an optimal gestational age, with advanced delivery techniques, such as the EXIT procedure, to afford the best possible outcome for the sickest of these patients.

This review outlines the current approaches to prenatal imaging, differential diagnosis, antenatal natural history, and available treatment options for the most commonly prenatally diagnosed malignant tumors.

NEUROBLASTOMA

Neuroblastoma is one of the most common tumors of infancy and childhood, with a clinical incidence of between 1 in 10 000 and 1 in 30 000 individuals. Three hundred cases of neuroblastoma have been suspected or diagnosed by prenatal ultrasound examination during the third trimester [1]. The primary tumor is often small and 90% of cases involve the adrenal gland, creating difficulties in distinction between the mass itself and the upper

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KEY POINTS

- Fetal MRI is a useful imaging tool when a fetal tumor is suspected.
- Diagnosis of a fetal tumor should prompt referral to a high-risk specialty center.
- In-utero interventions for fetal tumors are still under investigation.

pole of the ipsilateral kidney. Cystic and solid areas within the mass are typically seen, which may be related to hemorrhage into or necrosis of the tumor. Purely cystic lesions have also been reported in fetal neuroblastoma and may indicate a more favorable prognosis [1–3]. Calcifications within neuroblastomas are often described as microcalcifications with acoustic shadowing. The tumor is usually well encapsulated and may displace the kidney inferiorly and laterally but preserves the renal outline (Fig. 1). If arising in the sympathetic ganglia, the mass may be seen in the chest, cervical region, or intra-abdominal paravertebral locations. Cervical lesions sufficiently large to compromise the fetal airway have been reported, and large retroperitoneal masses presenting as flank masses which are readily palpable on physical examination have been reported. A suprarenal mass associated with hepatomegaly is highly suggestive of the diagnosis of neuroblastoma. Likewise, if a liver mass is seen on prenatal ultrasound examination, one needs to carefully examine all neural-crest regions, especially in the renal and suprarenal areas, to rule out a primary tumor locus [1].

Although most prenatally diagnosed neuroblastomas have a favorable prognosis, it appears there is a subset of neuroblastoma diagnosed *in utero* or in newborns which does display an aggressive biologic behavior. Among the 300 cases of fetal or perinatal neuroblastoma reported, 83% were stage I or II, but there were also one each with stage III and IV disease and five with stage IVS disease [1]. In addition, in the series by Jennings *et al*. [4], there were 14 stillbirths, 44 neonatal deaths, and two late deaths, with only 10 survivors. Eight cases were associated with metastases to the placenta and one had umbilical-cord metastases. However, the incidence of adrenal neuroblastoma *in situ* at neonatal autopsy has been reported to occur as frequently as in 1 of 40 patients dying from unrelated causes. Neuroblastoma *in situ* likely does not have the same malignant potential.

In cases of stage IVS disease, bluish subcutaneous nodules (the so-called 'blueberry muffin' sign) from metastatic neuroblastoma may be seen all over the infant's body. Among postnatal neuroblastomas, approximately 20% may release vasoactive peptides on palpation. The abdomen should be gently palpated to discern an abdominal mass and its relationship to other viscera. The liver

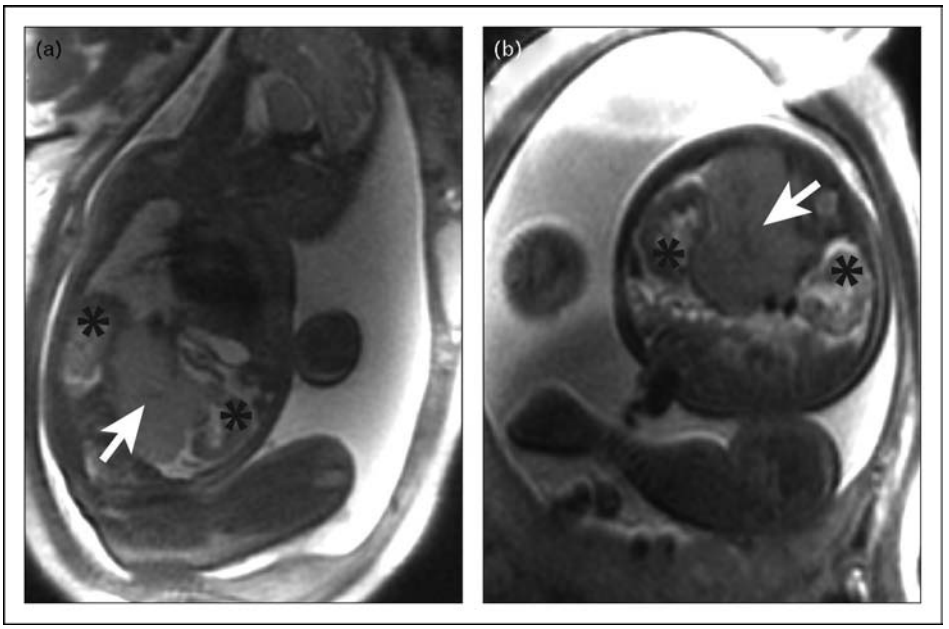

FIGURE 1. Fetal MRI demonstrating coronal (a) and axial (b) images of a large lobulated retroperitoneal mass with extension to the left lower thoracic paraspinal region (white arrow) with no obvious involvement of the kidney (asterisk), which is consistent with the diagnosis of neuroblastoma.

should be assessed for the size and evidence of metastases. The newborn with suspected congenital neuroblastoma should have plain radiography of the abdomen, chest, or neck region (depending on the tumor location). Neuroblastoma has characteristic finely stippled calcifications. Chest radiography should be performed to exclude pulmonary metastases. In most instances, a computed tomography (CT) scan is indicated to more accurately stage the disease and define the extent of the primary tumor. Urine should be collected for the spot measurement of catecholamines and tumor metabolites, including epinephrine, norepinephrine, dopamine, vanillyl mandelic acid, and homovanillic acid. Baseline liver function tests should be determined in all patients; even when the CT of newborn diagnosed with fetal neuroblastoma is without the evidence of hepatic metastases. Serum ferritin and neuron-specific enolase should be assayed, as they have prognostic significance in patients less than 1 year of age. As part of the preoperative staging, a technetium-99m bone scan, and bone marrow aspiration and biopsy, should be performed. ^{123}I-metaiodobenzylguanidine and ^{99}mTc-methylene diphosphonate scintigraphy can be useful in identifying the metastatic disease [5,6].

The child should undergo surgery for biopsy, staging, and resection of the primary tumor, if possible without jeopardizing adjacent structures. This will provide tissue for the determination of N-*myc* amplification and DNA ploidy. More than 90% of perinatal neuroblastomas have a DNA index of more than 1, which is associated with a better prognosis in infants. In addition, fewer than 5% of perinatal neuroblastomas have N-*myc* amplification [5,7,8].

Familial cases of neuroblastoma have been observed in siblings, identical twins, and one case in which the mother and child were both affected [9–14]. Neuroblastoma has also been reported in patients with the Beckwith–Wiedemann syndrome, pancreatic islet cell dysplasia, and infants born to mothers taking phenytoin.

The treatment of neuroblastoma depends on the clinical staging. In stage IVS disease, with the presence of diploid DNA complement and N-*myc* amplification, chemotherapy is indicated. In the absence of these findings, observation alone is appropriate. In stage I (primary with regional or distant metastases) or stage II (regional lymph node metastases but no distant metastases), surgery alone is sufficient. But in stage III (tumor extends beyond midline and bilateral lymph nodes may be involved) or stage IV (distant metastases), preoperative chemotherapy is indicated. Overall, the long-term survival in prenatally diagnosed neuroblastoma is over 90% [15]. There are currently no common indications for prenatal intervention.

MESOBLASTIC NEPHROMA AND WILMS' TUMOR

A mesoblastic nephroma is a rare tumor, but accounts for 3–10% of all pediatric renal tumors and is the most common renal tumor in infants under 3 months of age. Ninety percent of mesoblastic nephromas are diagnosed in the first year of life [16]. It has been estimated that fewer than 50 cases have been described *in utero*. The differential diagnosis of mesoblastic nephroma includes hydronephrosis and multicystic dysplastic kidney, focal renal dysplasia, and diffuse nephroblastomatosis and nephroblastoma.

Nephroblastoma (Wilms' tumor) accounts for 80% of renal neoplasms in children. Wilms' tumor has a peak incidence at 2–3 years of age, but it can present at any time from fetal life to adulthood. Several cases now have been diagnosed *in utero*. Wilms' tumor is associated with many genetic conditions, including Beckwith–Wiedemann, Denys–Drash, Klippel–Trenaunay syndromes and neurofibromatosis and the WAGR complex (Wilms' tumor, aniridia, genitourinary malformations, and mental retardation), suggesting a genetic predisposition to Wilms' tumor [17]. However, the most common presentation of Wilms' tumor is an asymptomatic abdominal mass. Abdominal pain, hematuria or malaise, weakness, anorexia, and weight loss may also be presenting symptoms.

The majority of mesoblastic nephromas prenatally diagnosed with ultrasound imaging present during the third trimester. Mesoblastic nephroma can present as a large (4–8 cm), unilateral renal mass with nodular densities or as diffuse renal enlargement. These tumors are predominantly solid, but cystic areas are occasionally seen, most likely because of hemorrhage with subsequent cystic degeneration. Unlike Wilms' tumor, there is no well-defined capsule. Many fetal mesoblastic nephromas are initially detected by the ultrasound examination because of a discrepancy between uterine size and gestational dates due to associated polyhydramnios. Fetal MRI has been reported to aid in the accurate prenatal diagnosis of mesoblastic nephroma. The advantages of MRI include better tissue contrast and definition of the relationship of the tumor to adjacent structures [18,19].

The sonographic features of Wilms' tumor may be indistinguishable from those of mesoblastic nephroma. Both present as complex masses that arise from or may completely replace the normal kidney. These tumors are predominantly solid, but

cystic areas also can be seen. There may be a well-defined pseudocapsule in Wilms' tumor as opposed to mesoblastic nephromas. In mesoblastic nephroma, polyhydramnios is a feature of most cases that have been reported. Few antenatally detected cases of Wilms' tumor have been described thus far, so it is uncertain whether polyhydramnios may also occur in association with Wilms' tumor. MRI may be used to enhance anatomic delineation and provide a better appreciation of the impact of a renal mass on adjacent structures (Fig. 2). Additionally, if bilateral renal lesions are diagnosed, it potentially suggests a diagnosis of Wilms' tumor rather than congenital mesoblastic nephroma [18].

LeClair *et al*. [20] found that almost half of newborns with mesoblastic nephroma delivered before 34 weeks of gestation. In addition, 25% of fetuses showed evidence of fetal distress prompting Cesarean section delivery. This same study found 22% of patients were hypertensive because of either renin production within the tumor itself or altered renal perfusion by mass effect of the tumor inducing renin production by the native kidney. The fetus with a suspected renal tumor should undergo a detailed sonographic evaluation to detect associated anomalies and clues to the cause of the mass. The features of Perlman syndrome, including fetal ascites, hepatomegaly, macrosomia, and polyhydramnios, should be sought [21]. Because of the benign nature of most mesoblastic nephromas, if ultrasound examination convincingly shows a renal lesion, it is recommended to allow the pregnancy to go to term. There appears to be a higher incidence of preterm labor and preterm rupture of membranes in pregnancies complicated by mesoblastic nephroma, as a result of associated polyhydramnios. Because of the risks of prematurity and potential for complications related to mesoblastic nephroma, it is recommended to deliver these patients in tertiary care centers to optimize care of the neonate. Similarly, for Wilms' tumor, the pregnancy should be followed closely, but because the polyhydramnios may not be present these fetuses potentially may have less of a risk for preterm labor. Additionally for Wilms' tumor, a family history should also be excluded and the contralateral kidney should be closely examined for anomalies or masses. These tumors seldom achieve a size that might preclude vaginal delivery; however, an ultrasound examination should be done close to term to assess this possibility.

The infant should be delivered in a tertiary care setting with consideration given to cesarean section delivery to obviate the potential for dystocia or hemorrhage into the tumor. Once the infant with a mesoblastic nephroma has been stabilized, further preoperative radiographic studies should delineate the size and extent of the mass. Surgical resection of the tumor is the therapy of choice for mesoblastic nephroma, and it is usually curative. The vast

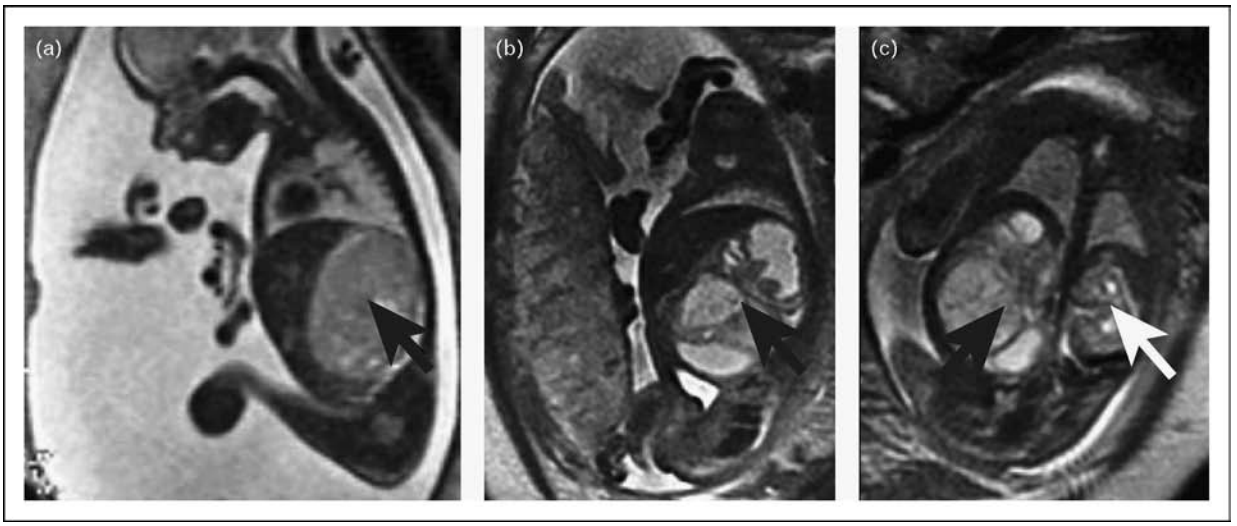

FIGURE 2. (a) Fetal MRI image showing a well-defined, homogeneously solid mass arising from the right kidney (black arrow). There was preservation of normal right renal tissue, and collecting system was noted posteriorly and inferiorly, which is consistent with the diagnosis of congenital mesoblastic nephroma. (b,c) Fetal MRI images demonstrating axial (b) and coronal (c) sections through the fetus showing a complex right renal mass (black arrow) with a dilated upper-pole collecting system with low signal mass extending into the collecting system. There is a lobulated heterogeneous high signal mass in the lower pole. There is no involvement of the contralateral kidney (white arrow) and the mass compresses the adjacent liver, but is separate. These findings are consistent with a Wilms' tumor.

majority of these patients do well, but should have close surveillance for recurrence during the first year. Hypercalcemia may also occur in mesoblastic nephroma as a paraneoplastic phenomenon because of the tumor production of parathyroid hormone-like peptides or prostaglandins causing hypercalcemia [22–25].

Some have suggested that the so-called cellular or atypical congenital mesoblastic nephroma should be treated as a potentially malignant tumor [26]. The cellular variant of mesoblastic nephroma carries no adverse prognostic significance in infants younger than 3 months of age. However, in older infants the demonstration of increased cellularity and high mitotic rate is of some concern because a few patients with such lesions will experience local recurrence or distant metastases. Infants older than 3 months of age with the cellular variant of congenital mesoblastic nephroma should probably receive adjuvant chemotherapy, whereas in infants younger than 3 months of age resection alone is adequate therapy [27,28]. The proper role for adjuvant chemotherapy in mesoblastic nephroma remains controversial [16], especially in infants less than 3 months of age in the presence of tumor spillage with the cellular variant. It is believed that cellular variants with genetic characteristics like *ETV-6–NTRK3* gene fusion associated with translocation between chromosomes 12 and 15 may respond better to chemotherapy [16]. In the setting of recurrent disease, combinations of vincristine, doxorubicin and cyclophosphamide or ifosfamide, carboplatin, and etoposide have been used successfully [29,30]. Chemotherapy can be used either alone or in combination with radiation therapy [31,32].

The affected newborn's blood pressure should be monitored, as 50% of Wilms' tumors may have associated hypertension. Associated anomalies (aniridia, cryptorchidism, and hypospadias) or physical signs of Beckwith–Wiedemann syndrome (macrosomia and macroglossia) should be excluded. A diagnostic work-up for the presence of metastases should include chest radiography and abdominal CT scanning. Abdominal ultrasound should be obtained to evaluate tumor thrombus within the renal vein and the inferior vena cava. A newborn with suspected Wilms' tumor should undergo an exploratory laparotomy for radical nephroureterectomy and exploration of the contralateral kidney to exclude synchronous bilateral lesions. In the National Wilms' Tumor Study-5 protocol, in cases of stage I Wilms' tumors that weigh less than 550 g in a patient younger than 2 years of age, a complete surgical resection is all that is necessary [33–35]. In other tumors, adjuvant treatment with chemotherapy and radiation therapy is planned according to stage of disease and histology as defined by the National Wilms' Tumor Study. Expected long-term survival rates of greater than 90% for localized cancers and approximately 70% for metastatic disease are achieved with current treatment regimens [36].

HEPATIC TUMORS

Tumors of the liver are rare during the perinatal period. They account for only 5% of all neoplasms that occur in the fetus and the newborn. The most common primary hepatic tumor is hemangioma, followed by mesenchymal hamartoma and hepatoblastoma [37,38]. However, metastatic lesions are more common than primary liver tumors. The most common tumor that metastasizes to the liver in the fetus and newborn is neuroblastoma, followed by leukemia, yolk-sac tumor from sacrococcygeal teratoma (SCT), and rhabdoid tumor of the kidney.

Hepatoblastoma is the leading primary hepatic malignant tumor occurring during the first year of life. Typically, hepatoblastoma presents as an upper abdominal mass arising from a single area, more often from the right lobe of the liver than the left. Hepatoblastoma can be detected by antenatal sonography. A broad range of congenital anomalies and malformation syndromes have been reported to occur in association with hepatoblastoma. Hemihypertrophy can occur in as many as 2–3% of affected patients. Beckwith–Wiedemann syndrome and intestinal adenomatous polyposis are the most commonly associated syndromes. The differential diagnosis of fetal hepatomegaly, usually involving splenomegaly as well, includes hydrops, fetal infection, anemia, metabolic abnormalities (e.g., hypothyroidism), and certain syndromes such as Beckwith–Wiedemann and Zellweger [37,38].

Hepatoblastoma developed during fetal life is rarely detected prenatally. Recent additions to the literature are mainly case reports [39▪,40▪]. Neonatal hepatoblastomas are typically solid and echogenic, and calcifications may be present. Fetal MRI may be of use in differentiating the cause of fetal liver masses [37,38] (Fig. 3). Hamartomas typically appear as an irregular cyst on ultrasound examination. Both oligohydramnios and polyhydramnios have been reported in association with mesenchymal hamartomas.

A pregnant woman carrying a fetus in which a hepatic tumor is suspected should undergo an extensive prenatal evaluation. This should include a detailed sonographic examination to define the nature of the mass, location, blood supply, and any associated anomalies. Color Doppler studies may be

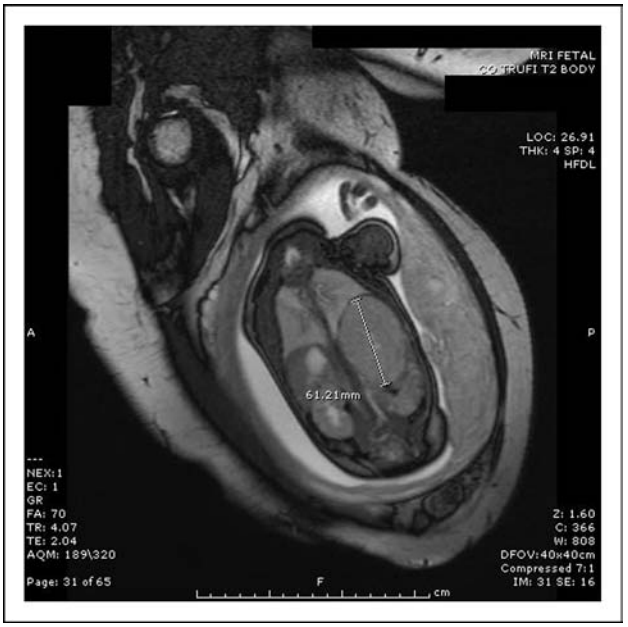

FIGURE 3. Fetal MRI showing a hepatic mass. Differential diagnosis includes hepatoblastoma and hemangioendothelioma.

helpful in distinguishing hemangioma from hepatoblastoma, mesenchymal hamartoma, or adenoma. Evidence of other hemangiomas should be sought. While mesenchymal hamartoma is usually an isolated finding, associated anomalies such as tracheoesophageal fistula and annular pancreas have been reported. A fetus with a hepatic tumor should be examined for the evidence of organomegaly or macroglossia, which may be indicators of Beckwith–Wiedemann syndrome. Every fetus with a hepatic mass should undergo echocardiography to obtain baseline combined ventricular output values and be followed for the development of high-output cardiac physiology. Pregnancies complicated by hepatic tumors should be delivered in a tertiary care center, with neonatologists, pediatric surgeons, and pediatric oncologists available. Depending on the size of the lesion, cesarean section may be necessary. Tumor rupture at the time of delivery has been reported with mesenchymal hamartoma and hepatoblastoma.

Once an infant with a hepatic tumor is born, attention should focus on establishing a definitive diagnosis using radiographic methods. MRI is a useful tool in establishing the diagnosis as well as determining the extent of the lesion. In the newborn with a hepatic mass suspected of being a hepatoblastoma, the serum α feto-protein (AFP) level should be measured. Surgical resection is the primary mode of treatment in hepatoblastoma. In cases of mesenchymal hamartoma, definitive treatment consists of a frozen section to confirm the diagnosis and exclude the possibility of malignancy and then complete resection of the mass. In hepatoblastomas that are found to be unresectable at operative staging, a biopsy is performed to make a diagnosis and chemotherapy is begun. Reexploration for the evidence of tumor regression with consideration of definitive resection occurs after several cycles of chemotherapy. In some centers, a decision on resectability is made on the basis of imaging studies, and a percutaneous biopsy is obtained to make a tissue diagnosis before starting chemotherapy. Surgical resection of liver tumors, whether hemangioendotheliomas, mesenchymal hamartomas, or hepatoblastomas, should be undertaken by experienced pediatric surgeons. In unresectable cases of hepatoblastoma, hepatectomy and liver transplantation achieves survival of 70–80% [41▪].

SACROCOCCYGEAL TERATOMAS

SCT is one of the most common tumors in newborns; however, it is still rare, occurring in 1 in 23 000 to 1 in 40 000 live births [42]. It is defined as a neoplasm composed of tissues from either all three germ layers or multiple foreign tissues lacking an organ specificity arising in the sacrococcygeal region. SCT has been classified according to the relative amounts of presacral and external tumor [43]. Type I is predominately external, type II arises externally and has a significant intrapelvic component, type III SCTs have abdominal extension, and type IV is presacral only. Malignant transformation has frequently occurred by the time a type IV SCT is diagnosed. The differential diagnosis of SCT includes lumbosacral myelomeningocele, neuroblastoma, glioma, hemangioma, neurofibroma, cordoma, leiomyoma, lipoma, and melanoma. The most common clinical presentation is uterine size greater than gestational dates, initiating an ultrasound examination [44]. Most SCTs are solid or mixed solid and cystic lesions. Most prenatally diagnosed SCTs are extremely vascular, which is easily demonstrated with the use of color flow Doppler studies. Polyhydramnios has been noted in most cases of prenatally diagnosed SCT, although the mechanisms for this are not known, it is likely secondary to renal hyperfiltration occurring as a result of high output state [44]. Fetal MRI is an imaging modality that can provide important anatomical detail in cases of SCT (Fig. 4). MRI may be particularly useful in defining the pelvic component of SCT and impact on other pelvic structures if there is polyhydramnios, oligohydramnios, hydronephrosis, or hydrocolpos [45].

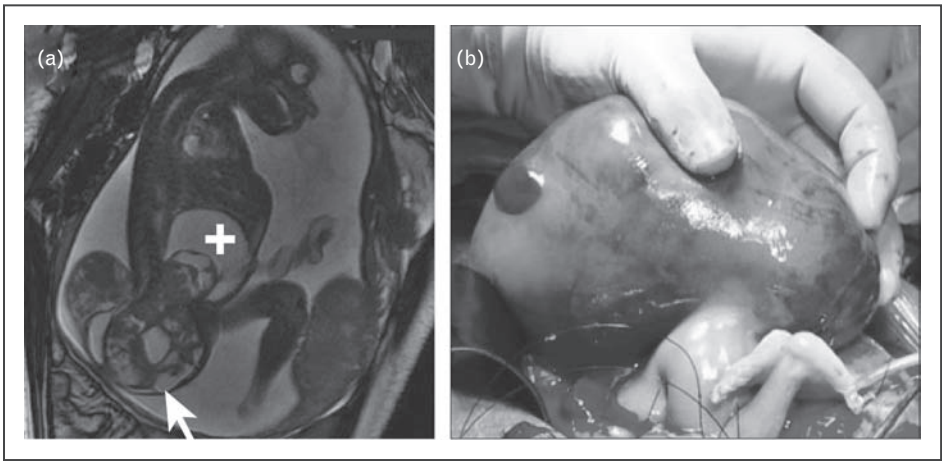

FIGURE 4. (a) Fetal MRI demonstrating a large solid and cystic presacral mass with an extensive extrapelvic component (arrow) in conjunction with intra-abdominal extension (plus sign). (b) In-utero resection for a fetus with a large sacrococcygeal teratoma associated with early signs of hydrops, placentomegaly, and impending high output cardiac failure.

While the mortality rate for SCT diagnosed in the newborn is at most 5%, the mortality rate for fetal SCT approaches 50%. Causes of fetal death include tumor rupture, hemorrhage into the tumor, high output cardiac failure (hydrops), and premature labor. Prognostic indicators are a current area of study. Weekly sonographic examinations should be performed during pregnancy to assess amniotic fluid index, tumor growth, fetal well being, and early evidence of hydrops. Serial Doppler echocardiographic evaluations should be performed in all patients to detect early signs of high-output state, as evaluated by an increased diameter of the inferior vena cava (>1 cm), increased descending aortic flow velocity (>120 cm/s), or increased combined ventricular output (>500 ml/kg/min for CVO) [46,47▪]. Evidence of the earliest signs of heart failure, placentomegaly, and hydrops should be sought, as these may progress rapidly and are harbingers of preterminal events. Tumor volume-to-fetal weight ratio may also be a useful prognostic tool. Fetuses with a ratio greater than 0.12 by 24 weeks of gestation have been found to have a poor outcome compared with those with a lower ratio [48▪].

Interventions aimed at preventing this high prenatal mortality are the focus of study at several centers. Timing of delivery is incompletely understood. A Japanese nationwide survey found early delivery to be associated with increased mortality [49▪]. Intuitively, large tumors and fetal demise will hasten premature labor and likewise have poorer prognosis. Alternatively, investigators at the Children's Hospital of Philadelphia recently reported better than anticipated survival in aggressively followed high-risk SCT patients who were delivered between 27 and 32 weeks [50▪]. Appropriate patient selection for early delivery may improve survival. For premature patients with early signs of hydrops or placentomegaly, resection *in utero* remains a viable option. Primary resection of the external portion of the tumor is performed with interval resection of the pelvic extension of SCT [45]. Occlusions of feeding arteries to the fetal tumor with radio-frequency thermal ablation (RFA) continue to be reported [51▪]; however, clinical experience has led to significant complications because of collateral tissue damage and any further study should proceed with great caution [52].

Although SCTs are usually benign, they are prone to local recurrence and have malignant potential. Surveillance for tumor recurrence is essential postoperatively. In SCTs, AFP levels are a useful marker for possible recurrence; a consistent downward trend in values should be observed until normal levels are reached by 1 year of age. We currently recommend that all newborns with SCT have serum AFP levels measured and physical examinations performed, including digital rectal examinations every 3 months. Such surveillance is recommended for at least 3 years [53]. If the SCT was nonfunctional, postnatal pelvic sonographic examinations should be obtained at similar intervals. An MRI should be obtained on at least a yearly basis. Any increase over previous AFP values should prompt investigation for possible recurrence. Factors that are thought to increase the risk of recurrence of SCT or development of malignant yolk sac tumor include immature elements and microscopic rests of malignant histology or incomplete resection. The chance of this recurrence was estimated at 11% by Derikx *et al.* [54]. Recurrence of the tumor, however, does not necessarily indicate the development of

malignancy. It should be treated as a premalignant lesion and excised. Even with malignant transformation of SCT, results with current chemotherapeutic regimens have achieved excellent survival rates. Misra *et al.* [55] reported survival rates of 88% with local disease and 75% even in the face of distant metastases. If the pathologic examination of the SCT reveals microscopic rests of endodermal sinus tumor, it remains controversial as to whether chemotherapy is indicated [56]. Older studies suggested any amount of yolk sac tumor presaged a poor prognosis and aggressive treatment was indicated [57,58]. More recent studies suggest the presence of yolk sac tumor, foci of fetal lines, and immature endodermal glands in the SCT are associated with an increased risk of recurrent disease [59,60]. These recurrences, however, are amenable to modern combination chemotherapy with excellent survival [56,58,61–63]. As there is no consensus on this issue, the decision to treat microscopic rests of yolk sac tumor with combination chemotherapy will vary from institution to institution.

CONCLUSION

Advances in prenatal imaging have increased the diagnosis of tumors in the fetus. Even so, these tumors are quite rare. Diagnosis of a tumor in the fetus should prompt referral to a high-risk specialty center for appropriate planning for delivery, as well as postnatal oncologic work-up. There are rare indications for fetal intervention. After delivery, the neonate undergoes standard oncologic evaluation and staging for the given tumor, with the majority having a good prognosis.

Acknowledgements

None.

Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- ■ of special interest
- ■■ of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 147).

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